AMENDMENTS TO THE SPECIFICATION

On page 1, lines 6-7, following -- December 21, 1999 --

please add:

-- -- and is a Divisional from non-provisional application US Serial No. 09/589,978 filed on June 7, 2000 -- --

Applicants hereby submit a marked version of Specification Replacement Sheet 1 to show changes made. Please enter the Replacement Sheet. The Replacement Sheet does not contain new matter.

[REPLACEMENT SHEET]

COMPOSITIONS AND METHODS FOR DRUG DELIVERY USING pH SENSITIVE MOLECULES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of prior provisional applications 60/137,859 filed on June 7, 1999, 60/167,836 filed on November 29, 1999 and 60/172,809 filed on December 21, 1999 and is a divisional application of 09/589,978 filed on June 7, 2000.

FIELD OF THE INVENTION

The present invention relates to the delivery of desired compounds (*e.g.*, drugs and nucleic acids) into cells using pH-sensitive delivery systems. The present invention provides compositions and methods for the delivery and release of a compound of interest to a cell.

BACKGROUND OF THE INVENTION

Drug Delivery

A variety of methods and routes of administration have been developed to deliver pharmaceuticals that include small molecular drugs and biologically active compounds such as peptides, hormones, proteins, and enzymes to their site of action. Parenteral routes of administration include intravascular (intravenous, intraarterial), intramuscular, intraparenchymal, intradermal, subdermal, subcutaneous, intratumor, intraperitoneal, and intralymphatic injections that use a syringe and a needle or catheter. The blood circulatory system provides systemic spread of the pharmaceutical. Polyethylene glycol and other hydrophilic polymers have provided protection of the pharmaceutical in the blood stream by preventing its interaction with blood components and to increase the circulatory time of the pharmaceutical by preventing opsonization , phagocytosis and uptake by the reticuloendothelial system. For example, the enzyme adenosine deaminase has been covalently modified with polyethylene glycol to increase the circulatory time and persistence of this enzyme in the treatment of patients with adenosine deaminase deficiency.

The controlled release of pharmaceuticals after their administration is under intensive development. Pharmaceuticals have also been complexed with a variety of biologically-labile polymers to delay their release from depots. These polymers have included copolymers of poly(lactic/glycolic acid) (PLGA) (Jain, R. et al. Drug Dev. Ind. Pharm. 24, 703-727 (1998), ethylvinyl acetate/polyvinyl alcohol (Metrikin, DC and Anand, R, Curr Opin Ophthalmol 5,